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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

NOTIFICATION DATE	DELIVERY MODE
06/15/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/829,250	HATTORI ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-18,20-24 and 32-41* is/are pending in the application.

4a) Of the above claim(s) *33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18,20-24,32 and 35-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed April 4, 2007 amending claims 18, 20-22 and 32, canceling claims 19 and 25-31 and adding claims 35-41 has been entered.

Claims 14-18, 20-24 and 32-41 are pending. Claims 33 and 34 have been previously withdrawn.

Specification

The disclosure is objected to because of the following informalities: It recites "an amino acid sequence shown in SEQ ID NOs: 1 or 2", wherein SEQ ID NOs: 1 and 2 are the nucleotide sequences (page 7).

Appropriate correction is required.

Claim Objections

The amended claims 18 and 20-22 are objected to because they recite "a native luciferase" (emphasis added). Claims 18 and 20-22 depend from claim 14 that recites "the native luciferase" (emphasis added).

Claims 37-40 are objected to because they do not comply with the Sequence Rules 37 CFR 1.821 through 1.825.

37 CFR 1.821(d) requires the use of assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences containing 4 or more specifically defined amino acids. Said sequences should be present in the Sequence listing and computer readable form thereof.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35 and 37-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants indicate support foe claim 35 at "page 6, lines 3-4 (species of organisms) and by Example 2 beginning at page 15 (amplification)" (Remarks of April 4, 2007, page 6). This is not agreed with because while there is support for the species of organisms and for a mutant luciferase from HEIKE firefly or GENJI firefly obtained using primers of SEQ ID NOs: 1 and 2, there is no support for mutant luciferases from other species that are obtained using primers of SEQ ID NOs: 1 and 2 (specification, page 7 and page 15). With regard to claims 37-40, Applicants indicate support for the amino acid sequence PXAVVVLX$_{490}$GKXMTE, in which X$_{490}$ is an amino acid other than glutamic acid and X is any amino acid by "the Sequence Listing SEQ ID NOs: 4, 6 and 8, which presents the sequences of a number of different luciferase proteins, taken with the knowledge of one of ordinary skill in the art who could align the various sequences

to derive the common structure shown in claims 37-40. The sequences recited in the claims match residues 483 to 497 of each of SEQ ID NOs: 4, 6 and 8" (Remarks, page 6). This is not agreed with because only 2 sequences of SEQ ID NOs: 4 and 6 comprise the above sequence, whereas SEQ ID NO:8 has glutamic acid at position 490. Moreover, two or even three sequences cannot provide support for "any amino acid" of which there are 20.

Thus there is no indication that mutant luciferases of claims 35 and 37-40 were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 14-18, 20-24, 32 and 35-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 is directed to a mutant luciferase of any structure and properties having at least one amino acid mutation and having resistance to a surfactant, wherein said luciferase retains at least 85% of its activity in the presence of 0.1% surfactant improved luciferase activity in the presence of a surfactant compared to a native luciferase. Claims 15-17 depend from claim 14 and limit surfactant to a cationic, a

quaternary ammonium salt and a benzalkonium chloride, respectively. Claims 18 and 20-22 depend from claim 14 and limit the source of the native luciferase. Claim 24 depends from claim 14 limits the mutation to the mutation at the position corresponding to position 490 of the GENJI or HEIKI firefly luciferase. Claims 32, 35 and 36 are drawn to a surfactant (or specifically benzalkonium chloride in claims 35 and 36) resistant luciferase produced by the various genetic engineering methods. Since the patentability of the product resides in the product, the luciferase of claims 32, 35 or 36 is equivalent to luciferase of claims 14 or 17 for the purposes of this rejection. . Claim 41 limits the source to the native firefly luciferase and the mutation to the mutation at the position corresponding to position 490 of HEIKI firefly luciferase.

Claim 18 depends from claim 14, where the native luciferase derived from Order Cleoptera. Claim 19 depends from claim 14 and limits the native luciferase to the family firefly. Claim 20 depends from claim 14 and limits the native luciferase to the family *Pyrophorus*. Claim 21 depends from claim 14 and limits the native luciferase to GENJI firefly, HEIKE firefly, North American firefly or Russian firefly. Claim 22 depends from claim 14 and limits the native luciferase to the derived from *Pynophorous plagiophthalamus, Arachnocampa luminosa* or Rail worm. Order Cleoptera includes several Families of organisms having different physiological and biochemical properties, which in turn comprise several genera of organisms having different physiological and biochemical properties. Firefly families comprise structurally different luciferases

Claims 23 does not limit the number of possible mutation while claim 24 while referring to the luciferase from Luciola lateralis (HEIKE) or Luciola cruciata (GENJI),

does not impart any limitation on the structure except for the mutation at position 490. Similarly, claim 41.

While claims 37-40 limit mutant luciferase to comprising the sequence PXAVVVLX$_{490}$GKXMTE, said sequence does not exhibit luciferase properties and the rest of the structure is not described.

Thus, the claims are drawn to or depend from an enormous genus of a mutant luciferase having at least 85% activity in the presence of a surfactant compared to the parent luciferase. Said genus of mutants is characterized by function.

Applicants disclose two mutants of *L. lateralis* luciferase having an improved activity in the presence of a surfactant having sequences of SEQ ID NOs: 4 and 6 that comprise mutation E490K. (These two sequences differ by the mutation at position 217 wherein SEQ ID NO:4 has A217L and SEQ ID NO:6 has A217I). Therefore, a representative number of a luciferase mutated at position 490 is two. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of having an improved activity in the presence of a surfactant and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 14-18, 20-24, 32 and 35-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mutant *Luciola lateralis* luciferases having the sequences of SEQ ID NO:4 or SEQ ID NO:6 that are mutated at position 490 and have at least 85% activity in the presence of 0.1% surfactant compared to the native luciferase and for mutant *Luciola cruciata* luciferases with corresponding sequences, does not reasonably provide enablement for a mutant luciferase having an unknown homology to SEQ ID NO:4 or SEQ ID NO:6 and having at least 85% activity in the presence of 0.1% surfactant compared to the native luciferase, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Claim 14 is directed to a mutant luciferase of any structure and properties (the number of possible mutations is not limited) having improved luciferase activity in the presence of a surfactant compared to a luciferase in which a mutation has not been introduced. Claims 14-18, 20-24, 32 and 35-41 are so broad as to encompass any mutant luciferase with an unknown possible low homology to the luciferase of *Luciola lateralis* having the requisite properties or any mutant luciferase with an unknown possible low homology to the luciferase of *Luciola lateralis* having the requisite properties in which the amino acid corresponding to residue 490 is substituted. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant luciferase enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein

determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of two mutant luciferases having one or two amino acids different compared with the wild-type sequence.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, i.e. multiple substitutions. The specification does not support the broad scope of the claims which encompass any mutant luciferase having the requisite property with an undisclosed homology to the luciferase of *Luciola lateralis* and any mutant luciferase with no or low homology to the luciferase of *Luciola lateralis* in which the amino acid corresponding to residue 490 of *Luciola lateralis* luciferase is mutated because the specification does not establish: (A) regions of the protein structure which may be modified without effecting luciferase activity; (B) the general tolerance of

luciferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any luciferase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

While it is possible to align the sequences, it is unpredictable what effect will have the mutation at position corresponding to position 490 in HEIKE luciferase, if the aligned sequence is not highly identical to the sequence of HEIKE luciferase.

With regard to claim 35, the use of primers of SEQ ID NOs: 1 and 2 would allow for obtaining only a luciferase fragment comprising position corresponding to position 490 not the entire active luciferase and only from highly homologous species. Thus, said primers can be useful for obtaining mutants of HEIKE or GENJI luciferases but not mutants that are not highly homologous thereto. In order to obtain said mutants residues 483-497 in the wild-type luciferase should be replaced with the amplified fragment.

With regard to claims 37-40 that limit the mutant luciferase to comprising the sequence PXAVVVLX$_{490}$GKXMTE, the effect of the rest of the luciferase structure is unpredictable and there is no guidance provided as to what the rest of the structure should be. As mentioned above, the sequence PXAVVVLX$_{490}$GKXMTE does not exhibit luciferase properties.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications

of any luciferase with no or low homology to the luciferase of Luciola lateralis having the desired properties in which the amino acid corresponding to residue 490 is or is not mutated. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of luciferases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step of ligating the obtained fragment into the plasmid encoding the full-length sequence of the luciferase.

Claim 41 is confusing as drawn to "A firefly luciferase" wherein a mutant luciferase obtained from a firefly luciferase appears to be intended.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 14-18, 20-24, 32 and 35-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Hirokawa et al.

The applied reference has a common assignee and one common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of

this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Hirokawa et al. (US Patent 6,074,859, form PTO-1449 filed April 22, 2004) teach mutant luciferases having improved activity compared with the wild type luciferase. The activity is measured in buffers containing surfactants such as HEPES, CHES, Mes, TAPS, ammonium sulfate, etc (for example, columns 12-13). Furthermore, Hirokawa et al. teach SEQ ID NO: 14 that has 99.8% identity to SEQ ID NO:4 and 99.7% identity to SEQ ID NO: 6 of the instant invention. SEQ ID NO:4 of the instant invention differs from SEQ ID NO:14 disclosed in the Hirokawa et al. patent only by substitution T219I. SEQ ID NO:6 of the instant invention differs from said sequence by two substitutions L217I and T219I. Both Hirokawa et al. sequences have E490K substitution. Said mutant luciferase has an improved activity compared with the wild-type luciferase in buffers containing surfactants. Hirokawa et al. teach methods for measuring ATP using luciferase (Example 5).

Response to Arguments

Applicant's arguments filed April 4, 2007 have been fully considered but they are not persuasive.

With regard to the 112, 1st paragraph written description rejection, Applicants argue that the 112, 1st paragraph written description requirements are met because "a description of the invention, as in this instance, by its chemical and physical properties, is an entirely adequate substitute for any structural description" (Remarks, page 7, 1st

paragraph). This is not persuasive because one property, if a relative value can be counted as such, does amount for "properties" moreover for correlation between function and structure. Applicants further argue that "In the present instance, the specification describes the mutant luciferases of the invention as derivatives of native luciferases known from the prior art that are mutated so as to exhibit retention of their enzymatic activity in the presence of surfactants. Examples of three such mutant enzymes that are completely structurally characterized are presented in the Sequence Listing (SEQ ID NOS: 4, 6 and 8). Furthermore, there is description in the specification of how to isolate additional mutant luciferases that retain their activity in the presence of a surfactant using site-directed mutagenesis by PCR and primers of sequences disclosed (SEQ ID NOS: 1 and 2, see Example 2). The specification further describes several organisms from which nucleic acids suitable as a template to prepare mutant luciferases of the invention using this method can be obtained" (page 7, last full paragraph). This is not persuasive because the genus of claimed mutant luciferases is not limited to mutant luciferases having the sequences that are highly homologous to the HEIKE luciferase sequence. As discussed above, SEQ ID NO:8 is the sequence of a wild type not a mutant HEKE luciferase. SEQ ID NOs: 4 and 6 are mutants derived therefrom that are highly homologous to each other and to SEQ ID NO:8. The issue of "how to isolate" is the issue of the enablement not written description. Furthermore, SEQ ID NOs: 1 and 2 do not encode enzymatically active fragments. Applicants further argue that "the new claims 37-40 include further description of partial structure of the claimed enzyme, reciting a minimal sequence spans an amino acid position (490) that is

deemed important to the function of the claimed protein" (page 8, penultimate paragraph). this is not persuasive because claim 35 is not limited to mutants of HEIKE or GENJI luciferases comprising a sequence containing a mutation at position 490. While in mutants of HEIKE or GENJI luciferases such mutation is important, its importance for luciferases of any structure is not evident or expected. Further, as discussed above, said minimal sequence exhibits neither the claimed property nor enzymatic activity. Applicants further argue that "case law makes it very clear that, as an alternative to describing an invention by structure, it is entirely appropriate to claim the invention in product-by-process terms. *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993). The present claims 32, 35 and 36 claim the instant invention in such terms and therefore, no structural limitation need be present in these claims" (page 8, last paragraph). This is not persuasive because the patentability of the product resides in the product not in the process unless the process imposes limitations on the product. With regard to the 112, 1st paragraph enablement rejection, Applicants argue that the claims are enabled because the level of ordinary skill in the art is high. While the level is high, the specification still required to provide the necessary guidance as to where to apply it. Applicants further argue that the amino acid residue corresponding to position 490 of the HEIKE or GENJI firefly luciferases is stated to be an important determinant of stability of activity in the presence of a surfactant. (This is residues 487 for the North American firefly luciferase, p. 7, line 8 of the specification). While said residue is important for the HEIKE or GENJI firefly luciferases, its importance is not shown and is unpredictable for mutants of luciferases that are significantly different in amino acid

sequences from the HEIKE or GENJI firefly luciferases. Applicants further argue that "The specification also discloses two oligonucleotides SEQ ID NOS: 1 and 2, that are useful for mutating the amino acid position 490 of a luciferase" (page 10, last paragraph). These primers will allow the amplification of a fragment only. In order to obtain the claimed mutant luciferase said fragment should replace the corresponding fragment in the wild type sequence. Applicants further argue that the state of the art is such that it allows for the alignment of sequences (page 11). While the art allows for the alignment of the sequences, it does not allow the effect of the mutation in a sequence that is not highly homologous even though it is possible to align it. Applicants further argue that "The amount of experimentation needed to practice the invention is not large" (page 11). Applicants further argue that "because of the ease of making large libraries of mutations and testing them for activity under various conditions, the art must be said to be predictable, as it is more likely than not that the practitioner can in fact find a large number of operable mutants" (page 12). This is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants useful as claimed mutant luciferases requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the

specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. The instant rejected claims all include many variants with more than minor modifications to the structure of a wide variety of parent enzymes, which themselves may have substantial structural differences. As such the amount of experimentation required to make and use the currently claimed scope is still deemed to be undue.

With regard to the 102(e) rejection, Applicants argue that "buffers disclosed by Hirokawa are not "surfactants" within the meaning of that term in the present application" (page 13, 1st paragraph). It is not agreed with because buffers used by Hirokawa are surfactants and are not excluded by the definition of the term in the present application. Applicants further argue that "the luciferase of Hirokawa would necessarily, not merely possibly, or even likely, retain their activity in the presence of surfactants. This is especially so in view of the Examiner's position that retention of biochemical characteristics of an enzyme in the presence of mutations is unpredictable" (page 13, 2nd paragraph). These arguments are contradictory to Applicants' arguments with regard to the 112, 1st paragraph rejections. The mutant luciferase disclosed by Hirokawa (SEQ ID NO:14) differs from SEQ ID NO:4 of the instant invention differs from SEQ ID NO:14 disclosed in the Hirokawa et al. patent only by a single substitution T219I. SEQ ID NO:6 of the instant invention differs from said sequence by two substitutions L217I and T219I. Both Hirokawa et al. sequences have E490K substitution. If Applicants argue that the mutant luciferase of Hirokawa does not meet

the requirements of the instant claims, they cannot argue that mutant luciferase having any sequence other than SEQ ID NOs: 4 and 6 of the instant invention meet the requirements of the claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

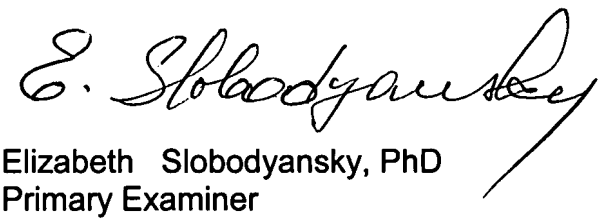
The post filing art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hattori et al. (2002) Biosci. Biotechnol. Biochem., Vol. 66 (12), pages 2587-2593, describe the instant invention. This is the work of the Inventors' Group.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

June 6, 2007